**Research Highlight**

Denosumab will play an important role in patients with solid tumours and bone metastases

Vera Hirsh

Chair, Lung cancer committee, McGill University, Royal Victoria hospital, Montreal, Quebec, Canada

Until recently, bisphosphonates, especially zoledronic acid (ZA), were considered standard treatment for prevention of skeletal related events (SREs) in patients with bone metastases. This trial compared the efficacy and safety of denosumab to ZA in the patients with advanced cancer (Excluding Breast and Prostate Cancer) or multiple myeloma (1).

Denosumab, a fully human monoclonal antibody which binds to and neutralizes RANKL, by it inhibiting osteoclast function and bone resorption, was non-inferior to ZA in delaying time to first on study SRE, HR=0.84, P=0.007. The superiority did not reach significant P-value, P=0.06, HR=0.9. Time to first and subsequent SREs by multiple event analysis showed also non-inferiority, HR=0.90, P=0.14. Overall survival (OS) and progression free survival (PFS) were similar in both groups, HR=0.95, P=0.43 and HR=1.00, P=1.00 respectively. Bone turnover markers were more suppressed with denosumab than with ZA, but the correlation of the degree of suppression with clinical benefit between these groups of patients is not available yet. Interestingly, when only solid tumours (excluding multiple myeloma) were analysed, denosumab showed superiority in delaying first on study SRE, HR=0.81, P=0.017 (2). Time to first and subsequent SREs was also superior for denosumab, HR=0.85, P=0.048.

Non-small cell lung cancer (NSCLC) was represented by 702 patients in this trial. The subanalysis of survival was reported at World Conference on Lung Cancer in 2011 (3) and it was superior on denosumab versus on ZA, HR=0.80, P=0.01. It is important to remember that we are dealing with a palliative group of patients, especially in case of lung cancer, who have only months to live. Quality of life, symptom control and good performance status are of great value for them and so is convenience of the drug administration. Subcutaneous versus intravenous injections and less of acute phase reactions are important assets of denosumab compared to ZA.

Renal function can deteriorate with Cisplatin, frequently administered in NSCLC treatments, forcing us to adjust the dosing of ZA. Zoledronic Acid requires regular monitoring of renal function, which is not necessary for denosumab.

On the other hand, familiarity and long experience with ZA, more data available on both preclinical and clinical anticancer activities, are also of importance to consider.

In conclusion, denosumab as a new antiresorptive agent will play an important role in patients with solid tumours and bone metastases.

**References**


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